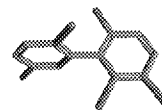


PCBs: ICF Status Report

October 22th, 2020



Raquel Silva
Cynthia Lin
Joanne Tigoveich
Steven Black
Nicole Vetter



Agenda for October 22nd, 2020

§ TO-37/TD-003

- § Neuro epi study evaluation
- § Neurotox HAWC extractions
- § Litstream updates
- § 2020 Literature update

§ TO-09/TD-008

- § Analysis of Co-eluting PCBs

■ TO-34 + TO-09/TD-003

- * ADME Screening, Extraction and Inventories (TO-34/TD-002, TD-005, TD-006)
- * Half-lives Manuscript (TO-34/TD-004)
- * MiST (TO-34/TD-003)
- * Evidence Map Manuscript (TO-34/TD-001, TO-09/TD-003)
- Budget update



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Literature screening & developing inventories

■ Tasks included in work plan (v3 sent and approved on 10/5)

1. Study evaluation

- Epi neuro studies
 - Batch 7 full team meeting occurred on 10/15 and ICF reviews were finalized by 10/16
 - Batch 8 preview file received from Pradeep and Sharon on 10/16 & 17; ICF's primary and secondary reviews began on 10/19 (due on 10/30); full team meeting scheduled for 11/12
 - Batch 9 preview assignment scheduled to be sent to Pradeep and Sharon on 10/26 (due 11/6); ICF primary and secondary reviews to begin 11/9
- Tox neuro studies
 - Batches 6a and 7a – Carrie working on Batch 7A

2. Data extraction (neurotox HAWC extractions).

- Pilot batch updated initial review submitted on 10/9, Excel file received from EPA on 10/21
- ICF internal training scheduled for 10/23, extractions next week, review meeting scheduled for 11/10
- Make Raquel, Ryan, Cynthia managers?
- Data already extracted?
- Questions about data extraction from figures (4 studies)
 - Example - Lilienthal, 1990, 198619. A few figures have results for different blocks or time intervals
 - Extract data points from these figures?
 - If so, to where? (block #/timepoints represented in HAWC).



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Literature screening & developing inventories

3. Reference tagging in litstream and HERO (ETC: 10/30)

- **Litstream™** - upload of health effect categories (2019 Update)
- **HERO** - apply/modify tags (2019 Update)

4. Update documentation and literature flow diagram (ETC: 11/6)

- Reports to be revised after reference tagging update.

5. 2020 Literature Update

- **Literature search update** (1764 Unique Results)
 - » References uploaded to HERO, source tags pending
 - » Corrections (n=10) being linked in HERO to the full text article as erratum
- **Title/abstract screening**
 - » 1725 references to be uploaded to SWIFT Active Screener
 - » Title-only references will be screened in litstream™ (n=29)
 - » Draft instructions and tag flowchart submitted on 10/21
 - » Draft form ready in SWIFT Active Screener



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Analysis of Co-eluting PCBs

- **Contractual documentation for Keri Hornbuckle and her team being finalized**
- **Schedule for bi-weekly meetings under review**



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ADME Screening and Extraction

▪ ADME Step 1

- Uploading tag updates – COMPLETED, 10/21
- Report delivery (ETC: 10/23)

▪ ADME Step 2

- Screening: COMPLETED
- Report delivery (ETC: 10/26)

▪ ADME Step 3: 2019 ADME Search (n=239) + 21 studies + legacy report

- Primary Screening: 239 + 21 studies completed
- QC: 239 studies completed + 21 studies (ETC: 10/22)
- Tertiary Review on 10% (ETC: 10/23)
- Report delivery – 2019 ADME Search (ETC: 10/26), legacy + 2019 (ETC: 11/2)

▪ Updated literature flow diagram – draft (ETC: 10/26), final (ETC: 11/2)

▪ 2020 Update (TD-006) – to be initiated in November



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ADME Screening and Extraction

* ADME Step 1 – 2019 Update

Relevant to ADME	402
Not Relevant to ADME	503
Other Supporting	1893
Abstract only	19
Foreign Language	2
Secondary Data Source	310
Exposure study	738
Physical/Chemical Properties	220
Species not PECO-relevant	802
Supporting Epi Study	0
Off Topic	3289
Total	6087

Number of Studies Flowing to Initial Categorization

	Secondary		
	Total	Data Source	Difference
Epi Hazard ID	231	130	101
Tox Hazard ID	233	55	178
Both Epi and Tox	71	43	28
Total	393	142	251



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ADME Screening and Extraction

» ADME Step 1 – 2019 Update

Supplemental Tags						
	Abstract only	Foreign Language	Secondary Data Source	Exposure study	Physical/Chemical Properties	Species not PECO-relevant
Abstract only	19			12		3
Foreign Language		2			1	
Secondary Data Source			310	111	17	3
Exposure study	12		111	738	43	11
Physical/Chemical Properties		1	17	43	220	4
Species not PECO-relevant	3		3	11	4	802



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ADME Inventory Update

- ✱ **Work plan to be submitted by 10/28**

- ✱ **Finalize inventories for pre-2019 ADME search**
 - ✱ **Human** – completed and reviewed by EPA under previous contract
 - ✱ **Animal** – completed under previous contract; **feedback expected by 10/30?**
 - ✱ **In vitro** (~40 studies) – to be completed after human and animal inventories, together with 2019 update

- ✱ **2019 ADME Search**
 - ✱ ICF compiling criteria for moving studies from ADME Step 3 to inventories



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MiST

- ✧ **Revised workplan to be submitted by 10/23**
- ✧ **MiST revision**
 - ✧ Revised tool and report submitted to EPA on 9/15, updated tool submitted on 10/1
 - ✧ Problem reported by Laura
("runtime error 1004. Activate method of worksheet class failed")
 - Likely cause: having multiple "activated" excel files open (e.g., macros enabled in more than one excel file at a time).
 - To options to address problem:
 1. **Update the Excel tool and User Guide** to alert users that other enabled Excel files should be closed prior to using MiST. This would require minimal LOE (approx. 1 hour).
 2. **Correct the code to fix this problem.** This will require more LOE and might be better to do in conjunction with additional revisions we will propose by email.
- ✧ **Materials and Methods section for Mixtures Manuscript**
 - ✧ Revised draft and literature flow diagram submitted on 10/9
- ✧ **User Guide**
 - ✧ Revised draft submitted on 10/1
- ✧ **Presentation for Public Science Meeting**
 - ✧ Waiting for EPA review of MiST and User Guide



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Half-lives Manuscript

* Follow-up questions:

1. Which keyword set will we use?
 - 28 unique keywords that captured relevant studies
 - 24 critical keywords
2. We excluded studies harboring “printed circuit board” in the original analysis. Since then, we have expanded our list of exclude terms that use the “PCB” acronym. Shall we use our expanded list in the KAT approach for the literature update?

Counts of Relevant, Not Relevant and Critical Keywords	
Total Number of Keywords Used in KAT	64
Number of Keywords that Captured Relevant Studies	28
Number of Critical Keywords	24
Number of Keywords that Failed to Capture Any Relevant Studies	36



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Evidence Map Manuscript – Draft Sections Progress

Health Effect Category	Assigned to	Status
Cardiovascular	Alexander Sergeev (epi), Michal Toborek (tox)	Tox draft submitted on 10/7 (needs revision)
Dermal	Robyn Blain	Final draft (completed)
Developmental	John Meeker (epi), Aileen Keating (tox)	EPA to provide feedback on revised draft
Endocrine	Michael Bloom (epi), Joanne Trgovcich (tox)	Revised draft submitted on 9/24
Gastrointestinal	Evan Coffman (epi), Brandall Ingle / Joanne Trgovcich (tox)	Final draft (completed)
Hepatobiliary	Evan Coffman (epi), Larry Robertson (tox)	Final revision in progress.
Immunological	Todd Jusko (epi), Geniece Lehmann (tox)	Epi outline/draft in progress (ETC: 10/26)
Metabolic	Alexander Sergeev (epi), Michal Toborek (tox)	Epi preliminary draft revised; Tox draft to start after cardiovascular (ETC: 11/1)
Musculoskeletal	Cynthia Lin (epi), Kelly Shipkowski (tox)	EPA to provide feedback on revised draft
Neurological	Pradeep Rajan & Sharon Sagiv (epi), Pam Lein & Carrie Klocke (tox)	EPA provided feedback on 10/1. Revised draft in progress (ETC: 11/6)
Ocular	Robyn Blain	Final draft to be revised given new studies in inventory
Reproductive	Pam Factor-Litvak (epi) Erin Yost (tox), Xabier Arzuaga (tox)	EPA provided Epi draft – male, based on outline, on 10/20 Waiting for Epi outline - female and reviewed draft - male (ETC: 10/26)
Respiratory	Raquel Silva (epi), Samantha Snow (tox)	Final draft to be revised given new studies in inventory



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Budget, as of 10/16/2020

TO/TD	Budget Hours	Budget \$	Current Hours	Current \$	Cumul. Hours	Cumul. \$	Remain. Hours	Remain. \$
TO-34							72%	71%
Total								
Tasks 18								
TD-00								
(EM								
TD-00								
(ADME								
TD-00								
(MIST								
TO-37								
TD-00								
(WP v3								

Ex. 4 CBI

▪ **TO-34:**

- TD-001 – Workplan v2 approved on 7/31
- TD-002 – Workplan v2 approved on 9/28
- TD-003 – Workplan v1 approved on 8/3; under revision

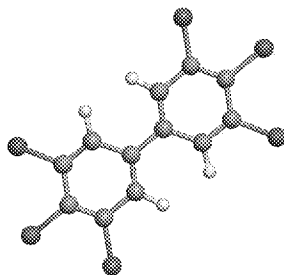
▪ **TO-37/TD-003**

- Workplan (v1), approved on 7/10
- Addendum received on 8/5, WP (v2) approved on 9/22
- Addendum 2 received on 9/18, WP (v3) approved on 10/5



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ICF Status Report

October 22nd, 2020

